REMARKS

Reconsideration of the above-identified application, in view of the following remarks, is respectfully requested.

I. Status of the Claims

Claims 1, 4 – 28, 94, 95, and 100 - 103 are currently pending in this application and are at issue. Claims 29 – 34 are withdrawn. Claims 1, 24, 29, 30, and 33 are amended and claims 2 – 3 and 91 are canceled herewith without prejudice. Claims 100 – 103 are new. Support for the amendments to claim 1 can be found in claim 94 as filed. Support for the amendment to claims 24, 29 and 30, 33, and 34 can be found in claim 95 as filed. Support for new claims 100 and 102 can be found in paragraphs 104 – 105. Support for new claims 101 and 103 can be found in paragraph 105, fourth line. No new matter has been added.

II. Rejections under 35 U.S.C. 103(a)

Schacht

Claims 1, 4, 15-28, 94, and 95 remain rejected as obvious under 35 U.S.C. §103(a) over Schacht (U.S. Pat. 6,933,328). The Examiner states that Schacht discloses a crosslinkable prepolymer, a polymer, and a mineral biologically active component for bone implant, and that compositions containing a bone substitute are taught in Schacht Examples 7 and 21. The Examiner then argues that it would be obvious to modify the Schacht process of placing the curable composition on top of an allograft filling and apply a mixture of the curable composition and allograft to form the compositions of the presently claimed invention.

Applicants respectfully traverse. Schacht does not provide a prepolymer comprising an anhydride of either a monomer or oligomer of a diacid or multifunctional acid. He, in fact, teaches against using such a prepolymer in his invention. While, as suggested by the Examiner, some disadvantages of the anhydride disclosed in Schacht can be overcome (i.e., by indirectly incorporating any reactive therapeutic agents), there is nothing in either Schacht or the knowledge of one of ordinary skill in the art that would suggest altering the Schacht formulation to include an anhydride of either a monomer or oligomer of a diacid or multifunctional acid in the to create the composition of the presently claimed invention. Further, while Schacht does provide radical initiation and light as initiators of the polymerization, there is nothing to suggest the particular combination of an anhydride, a carboxylic acid

molecule, chemical polymerization combined with light-initiated polymerization, and the use of a bone substituted admixed with the polymer. It would not have been obvious to one of ordinary skill in the art to combine these particular elements, particularly since Schacht taught against using an anhydride.

Further, an inventor of the presently claimed invention, in cooperation with Dr. Huys and Dr. Schacht, attempted to form a new bone implant and studied the usefulness of this bone implant in animal models (the Huys study) for dental and orthopedic use. The results of this study are discussed by Dr. Robert Langer in the Declaration submitted herewith. The Huys study tested the efficacy of a composition comprising the crosslinkable prepolymer as described by Schacht in combination with the bone substitute HTR®. As described by Dr. Langer, the results of this study indicate that, even when the Schacht process is modified so as to be mixed with a bone substitute, the composition has unsatisfactory clinical osseointegration. Dr. Langer states that the curable composition of the polymers disclosed in the Schacht patent mixed with the bone substitute Bioplant® HTR® is unacceptable as a bone implant material.

The compositions of the presently claimed invention using both light and chemical hardening were then developed. A pilot study (the Yukna study) demonstrating the usefulness of the bone implant material as presently claimed was performed in rabbits. This study is described by Dr. Langer as having good clinical osseointegration. These studies, though directed to dental use, are equally valid for other orthopedic applications. Claims 1, 4, 15-28, 94, and 95 as presently amended each require a polymer that is immediately hardening and requires the use of both a photoinitiator and redox chemistry using an anhydride polymer. These elements were successfully tested in the Yukna study. Comparatively, the Huys study provides significantly worse results. Since a mixture of bone substitute material and a crosslinkable polymer can produce such dramatically different results in as an implant or graft material, one skilled in the art would not be able to predict how Schacht's materials should be modified. Therefore, Schacht does not make the compositions or methods of the present invention obvious.

Further, the entire Schacht publication is directed to polymers that overcome the problem associated with the acidic polymer matrix. There is no reason provided either in Schacht or available to one of ordinary skill in the art to substitute a polymer such as the acidic methacrylic acid dianhydride described in Anseth or Shastri as part of IPN within the Schacht single polymer since the Schacht polymer was designed particularly NOT to encompass an acidic linkage. Furthermore, while Schacht used his own specific polymers not having an acidic linkage, the present invention provides a novel means of overcoming the potential acidity problem associated with the anhydride polymers. Bioplant® HTR® and calcium carbonate are both alkaline and both act to neutralize any acidity in the composition.

Without some rational reason to combine the anhydride polymer and bone substitute as presently claimed, the obviousness rejection cannot be maintained. "Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness" *KSR Int'l Co. v. Teleflex, Inc.*,127 S. Ct. 1727, 1741 (2007) quoting from) *In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006)

Schacht in view of Anseth or Shastri

Claims 5 – 14 remain rejected as obvious under 35 U.S.C. §103(a) over Schacht in view of Shastri et al. (US 5,837,752) or Anseth et al. (US 5,902,599). The Examiner argues that, while Schacht does not teach the methacrylic acid dianhydride polymer, the curable polymers described by Shastri or Anseth could be combined with the teaching of Schacht.

Applicants respectfully traverse. One of ordinary skill in the art would have no reason to modify the teaching of Schacht and combine it with either Shastri or Anseth, since the result of such a combination would be unpredictable. In fact, the Schacht polymer, when combined with a bone substituted, as described in the Huys study discussed Dr. Langer's declaration, did not work. Even if the Schacht teachings were modified as taught by Shastri or Anseth, a bone substitute having acceptable osseointegration would not have been formed.

Further, while there are many type of polymers and non-polymeric materials that can be used in some capacity for bone repair, the Schacht polymers are not analogous to the anhydride semi interpenetrating networks (IPN) described by Shastri and Anseth and cannot be defined as having interrelated teachings. The IPNs comprise two chemically distinct polymers which are physically inter-connected. In contrast, Schacht teaches the formation of a single polymer formed by polymerizing ether and/or ester linkages of prepolymers having at least two polymerizable end groups. Since single polymers and IPNs have significantly different formations, characteristics, and use, the single multifunctional polymer and the IPN are not, as the Examiner suggests, analogous art. In addition, the Schacht polymers are hydrogels, which expand upon exposure to water whereas the Shastri and Anseth IPNs are not. While "design incentives and other market forces can prompt variations of [a work], either in the same field or a different one," in the present case, the substitution of an IPN for a single polymer is not a "predictable variation" that a person of ordinary skill in the art can implement." *KSR Int'l Co. v.*

Teleflex, Inc., 127 S. Ct. 1727, 1741 (2007). Therefore it would not have been obvious to use the ethylenically unsaturated macromers of Shastri or Anseth in forming the compositions of Schacht.

Anseth in view of Schacht

All claims remain rejected under 35 U.S.C. §103(a) as obvious over Anseth in view of Schacht. The Examiner states that Anseth teaches that the biodegradable polymer networks can be combined with fillers, reinforcing materials, and/or other materials needed for a particular implant, and this teaching can be combined with the teaching of bone substitutes in Schacht.

Applicants respectfully traverse. The teaching of Anseth, namely that the prepolymers can be combined with fillers, reinforcement materials, radio imaging materials, excipients, or other materials as needed for a particular implant application, would not have made the present invention obvious. There is no suggestion in Anseth that a bone substitute should be combined with the prepolymers. Further, there would be no reason to combine Anseth with Schacht, since there was no evidence at the time of the invention that the Schacht polymers in combination with a bone substitute would work, and the test results in fact show that they do not work. Further, Schacht teaches against using the anhydride polymers.

The presently claimed invention requires that the polymer be immediately hardened by using both photoinitiator and redox chemistry. The polymers as described by Anseth in combination with Bioplant® HTR® were tested in animal models (the Brooks study) and discussed by Dr. Langer. Without the immediate hardening as provided in the presently claimed invention, the anhydride polymer combined with HTR® caused tissue necrosis and, in some instances, death to the animal.

III. Conclusion

In view of the above amendments and remarks, applicants believe that each of the pending claims in this application is in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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